Two Cases of Very Late Stent Thrombosis After Implantation of a Sirolimus-Eluting Stent Presenting as AMI

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SUMMARY

Stent thrombosis after sirolimus-eluting stent (SES) implantation has been reported to occur at 6 hours to 26 months after the procedure and usually within 2 weeks after discontinuation of antiplatelet medication.1-4) However, there are very few reports of stent thrombosis after 2 years. We report 2 cases of very late stent thrombosis after implantation of a sirolimus-eluting stent presenting as acute myocardial infarction (AMI). These late thromboses occurred about 2 years after SES implantation and over 1.5 years after discontinuation of ticlopidine. (Int Heart J 2007; 48: 393-397)

Key words: Drug-eluting stent, Stent thrombosis, Sirolimus

FOUR week therapy with ticlopidine or clopidogrel, in addition to aspirin, is currently standard care after percutaneous coronary intervention (PCI) with bare metal stent implantation (BMS). The recent availability of drug-eluting stents (DES), which dramatically reduce restenosis at the site of PCI, has again raised the issue of stent thrombosis. Stent thrombosis is a rare but potentially fatal complication of percutaneous treatment of coronary disease. Traditionally, stent thrombosis has been regarded as a complication of PCI during the first 30 post-procedural days. However, delayed endothelialization associated with the implantation of DES may extend the risk of thrombosis beyond 30 days. Its occurrence after DES placement has raised concerns, especially when it occurs late after the stent implantation. The mechanism of late thrombosis after DES is not yet completely understood. It is reported that angiographically proven late thrombosis occurs with an incidence of 0.35% to 0.7%.4,5) Independent predictors of stent thrombosis are premature antiplatelet therapy discontinuation, renal failure, bifurcation lesions, diabetes, and a lower ejection fraction.4-8) Here, we report
2 cases of very late stent thrombosis after implantation of a sirolimus-eluting stent (SES) presenting as AMI. These cases of late thrombosis occurred about 2 years after SES implantation.

Case 1: A 68-year-old female with a history of hypertension and diabetes mellitus was referred for coronary angiography after a recent inferior myocardial infarction and evidence of myocardial ischemia. Her coronary risk factors were controlled relatively well by Ca-antagonists and voglibose. Coronary angiography (CAG) showed a significant stenotic lesion in the mid-segment of the LAD and total occlusion of the proximal RCA. Primary PCI was undertaken with implantation of a bare metal stent (Multilink Zeta stent 3.5 × 28 mm) for proximal RCA. Ten days later, she underwent PCI for a mid LAD lesion with a sirolimus-eluting stent (SES, 2.5 × 23 mm). The angiographic result was excellent. Before PCI, the % diameter stenosis (%DS) was 92% and lesion length was 17 mm by quantitative coronary arteriography (QCA). The postprocedure %DS was 9%. A small diagonal branch originated from the stenotic lesion. We performed intravascular ultrasound during the procedure. After PCI, the intrastent minimal lumen area (MLA) was 3.9 mm² and there was no stent malapposition or stent fracture. Ticlopidine (200 mg) was prescribed for 3 months and 100 mg of aspirin daily was continued. One year after implantation of the SES, CAG showed no restenosis in either stent. Twenty-six months after implantation, she developed acute chest pain and her resting ECG showed ST elevation in the V2-5 leads. She was immediately referred for angiography the same day. In-stent thrombosis was observed at the entrance of the proximal SES in the LAD lesion. No restenosis was detected in BMS. After intracoronary aspiration thrombectomy, TIMI 3 coronary flow was achieved. She was treated by balloon angioplasty for LAD.

Figure 1. Coronary angiography of case 1. A: Baseline coronary angiography showing significant lesion in the mid-segment of the left anterior descending (LAD) coronary artery. B: Postprocedural coronary angiography after PCI with sirolimus-eluting stent (SES) in the LAD. C: Coronary angiography 26 months after the procedure showing total occlusion at the proximal edge of the SES.
Case 2: A 75-year-old, hypertensive male patient was referred to our hospital with stable angina pectoris. His blood pressure was controlled relatively well by Ca-antagonists and diuretics. CAG showed a culprit RCA with multiple lesions. Before PCI, QCA revealed %DS was 89% in the proximal and 83% in the mid portion, and lesion length was 16 mm in the proximal and 14 mm in the mid portion. Both lesions were relatively simple lesions. Elective PCI was undertaken with implantation of 2 SES (proximal; 3.5 × 23 mm, mid; 3.5 × 18 mm), and post %DS was 12% in the proximal and 10% in the mid portion. The procedure was uneventful. Ticlopidine (200 mg) was prescribed for 3 months and 100 mg of aspirin daily was continued. Ten months after SES implantation, CAG showed no restenosis in either stent. Twenty-two months after SES implantation, he presented to our hospital with the sudden onset of severe chest pain. An ECG showed ST elevation in leads II, III, and aVF. He was examined by CAG the same day. In-stent thrombosis was observed at the entrance of the proximal SES in the RCA lesion. TIMI 2 coronary flow was attained after intracoronary aspiration thrombectomy. He was treated by balloon angioplasty and we were able to achieve TIMI 3 coronary flow.

DISCUSSION

These 2 cases involved very late stent thrombosis after implantation of a sirolimus-eluting stent presenting as AMI. Stent thrombosis is a rare, but very serious and potentially fatal complication of PCI therapy. Its estimated 30-day mortality ranges from 20% to 48% and can cause myocardial infarction in 60% to 70% of patients.8,9)
We diagnosed these 2 cases as late stent thrombosis because there was no restenosis 1 year after stent implantation, total occlusion of the coronary artery happened at the entrance of the proximal SES, and we were able to remove the thrombus by successful intracoronary aspiration therapy.

Stent thrombosis in a DES is a serious complication associated with high mortality and sudden cardiac death. It can occur acutely, subacutely, or late. Late stent thrombosis has conventionally been defined as that occurring after the first 30 days following PCI. Although the mechanisms behind the acute and subacute stent thrombosis after BMS and DES are very similar, the reasons for late thrombosis after DES have yet to be completely understood. Some clinical features, such as premature antiplatelet therapy discontinuation, renal failure, diabetes, and lower ejection fraction, as well as procedure related observations, such as bifurcation lesions, stent underexpansion, and residual reference segment stenosis have been identified as independent predictors of late thrombosis.5-7) There have been early concerns about delayed healing and polymer related hypersensitivity reactions, with consequent risks of delayed thrombosis after DES implantation.10,11) SES effectively reduce restenosis by inhibiting neointimal hyperplasia, but they also delay the healing process far beyond the 3-6 month period usually required with bare metal stents. Impaired intimal healing is a recognized cause of late stent thrombosis in humans.10-12)

Pathologic studies have provided evidence of hypersensitivity vasculitis within the stented arterial segment after SES implantation with polymer fragments surrounded by giant cells and eosinophils.13) Delayed endothelialization of the stent strut is commonly considered to be the main causal factor for thrombosis, but local inflammatory reaction seems also to play a role. Indeed, late incomplete stent apposition and Frank aneurysm formation with eosinophilic infiltrates, likely caused by a hypersensitive reaction to the polymer coating of the stent, were observed in fatal cases.10)

To the best of our knowledge, the most delayed case of SES thrombosis is 26 months after stent implantation.4) Our cases occurred 26 months and 22 months after SES implantation.

The majority of the late thrombosis occurred just after discontinuation of antiplatelet therapy. However, in our 2 cases, the thrombosis happened over one year after premature discontinuation of ticlopidine. This suggested that another mechanism in addition to antiplatelet therapy might be responsible for the late stent thrombosis. One possible mechanism could be hypersensitivity to the stent polymer. The report of a CYPHER related death to the US FDA mentioned there was hypersensitivity to the CYPHER stent.14) DES without polymers may be beneficial in preventing late thrombosis.

In conclusion, evidence of very late stent thrombosis with the use of SES
was demonstrated in the present 2 case reports, and argues in favor of prolonged antiplatelet medication including ticlopidine in this setting. We have reported 2 cases of very late stent thrombosis after implantation of a sirolimus-eluting stent presenting as AMI. These late thromboses occurred about 2 years after SES implantation and over 1.5 years after discontinuation of ticlopidine. These results suggest there may be a mechanism other than discontinuation of antiplatelet therapy that is responsible for the late thrombosis. On the other hand, however, a permanent dual antiplatelet therapy could prevent thrombus formation in these cases. Better and improved antiplatelet therapy after DES implantation, especially the time of discontinuation of ticlopidine, needs to be developed.

REFERENCES